REMARKS

Applicants are filing a Request for Continued Examination (RCE) along with the present response. Claims 54, 55, 57 to 60, 81 to 84, 96, 120 to 122, and 124 to 143 are pending. Applicants have cancelled claims 85, 88, 94, 100, 107, 115 to 117, 119, and 123 without prejudice or disclaimer. Claims 1 to 53, 56, 61 to 80, 86, 87, 89 to 93, 95, 97 to 99, 101 to 106, 108 to 114, and 118 were previously canceled. Applicants have amended claims 54 and 55 to recite the claimed subject matter with greater particularity. Applicants have also added new claims 124 to 143. Support for the amendments and new claims can be found throughout the specification as originally filed, *e.g.*, at page 6, line 30; page 7, lines 1 and 2; page 29, lines 7 to 18; page 40, line 7; and at page 43, line 1; and in Examples 10 to 13. Applicants have also amended the specification to correct two obvious typographical errors. One of ordinary skill in the art would clearly have recognized the specification as filed included these errors. Thus, the amendments and new claims add no new matter.

Furthermore, applicants note that they have amended claim 54 to incorporate many of the elements of claim 123, now canceled. Claim 123 was not rejected over the prior art and applicants submit that claim 54, as amended, should now also be free of the prior art. In particular, amended claim 54 recites methods of inducing an immune response against human immunodeficiency virus (HIV) or an HIV epitope in a primate, the method comprising administering to the primate a nucleic acid composition comprising (a) at least four sets of nucleic acid molecules encoding wild-type HIV gp120 envelope glycoproteins, wherein the sets of nucleic acid molecules encode glycoproteins from primary isolates B715, Ba-L, and Czm, and from a clade E primary isolate, and (b) a set of nucleic acid molecules encoding a wild-type HIV gag protein from a primary isolate. Applicants note that claim 54 and its dependent claims are fully described in the application, e.g., at least in Example 12 of the specification, as originally filed. Furthermore, in an Information Disclosure Statement filed on July 11, 2006, applicants submitted a peer-reviewed publication (Pal *et al.*, *Virology* 348, 341-353, 2006) that describes the methods now claimed.

New claims 126 to 143 are drawn to methods of inducing an immune response against HIV or an HIV epitope in a human comprising administering the vaccine composition designated "DP6-001" (*see, e.g.*, page 6, last paragraph; and Examples 13 to 16). Claim 126 is analogous to claim 54, except that claim 126 is drawn to methods involving humans. As in claim 54, applicants have also incorporated specific nucleic acid and protein compositions previously recited in claim 123 into claim 126. Because the Office has determined that claim 123 is nonobvious, claim 126 should also be nonobvious for at least the same reasons. Applicants also respectfully draw the Office's attention to their publication (Wang *et al.*, *Vaccine* 26, 3947-3957, 2008), which further describes the claimed methods.

Telephonic Interview

Applicants' representatives thank Examiner Peng for conducting a telephonic interview on June 22, 2010. During the interview, the undersigned discussed the current claim rejections and potential claim amendments, as well as how those amendments would distinguish the prior art. However, no agreement as to the claims was reached.

Withdrawn Rejections

Applicants acknowledge that the prior rejection of claims 54, 55 to 60, 81 to 85, 88, 94, 96, 100, 107, and 115 to 122 under 35 U.S.C. § 112, ¶ 1 has been withdrawn.

35 U.S.C. § 112, ¶ 2

Claim 123 was rejected at page 2 of the Office Action mailed August 27, 2009 (the "Office Action") as allegedly indefinite. Applicants do not concede that claim 123 is indefinite. Nonetheless, in the interests of expediting prosecution, applicants have canceled claim 123. Applicants therefore request that the present rejection be reconsidered and withdrawn.

35 U.S.C. § 112, ¶ 1

Claim 123 was rejected at page 3 of the Office Action as allegedly containing new subject matter for reciting "primary isolates A,... and E." Applicants do not agree that claim 123 introduces new subject matter, however, as noted above, claim 123 has been canceled. Accordingly, the rejection should be withdrawn.

Claims 54, 55, 57 to 60, 81 to 85, 88, 94, 96, 100, 107, 115 to 117, and 119 to 123 were rejected because, according to the Office Action at pages 3 and 4, "the specification, while being enabling for a method of inducing an immune response to an HIV epitope in human, does not reasonably provide enablement for a method of inducing a protective immune response against a current or future HIV infection in humans." Applicants do not concede that the rejected claims are not enabled. Nonetheless, applicants have canceled claims 85, 88, 94, 100, 107, 115 to 117, 119, and 123, rendering the rejection moot as to those claims.

To the extent that the above rejection may be applied to amended claims 54, 55, 57 to 60, 81 to 84, 96, and 120 to 122, and to new claims 124 to 143, applicants respectfully traverse. Independent claims 54 and 126 recite methods of inducing an immune response against HIV or an HIV epitope in a primate or a human, respectively. Applicants have provided ample guidance to induce an immune response against HIV or an HIV epitope throughout the specification (*see, e.g.*, Examples 10 to 16). Further, the Office has already conceded that methods of inducing an immune response against HIV or an HIV epitope are adequately enabled (*see,* Office Action at pages 3 and 5 to 7). Thus, applicants respectfully submit that claims 54, 55, 57 to 60, 81 to 84, 96, 120 to 122, and 124 to 143 are adequately enabled. Accordingly, applicants request that the Examiner withdraw this rejection.

35 U.S.C. § 103(a)

Claims 54, 55, 57 to 60, 81 to 85, 88, 94, 96, 100, 107, 111 to 117, and 119 to 122 were rejected as purportedly unpatentable over Barnett *et al.* (*Vaccine* 15:869-873; "Barnett"), Nabel *et al.* (WO 02/032943; "Nabel"), Gao *et al.* (*J. Virol.* 70:1651-1667; "Gao 1"), Gao *et al.* (Meeting Abstract, *AIDS Vaccine 2001* Abstract No. 201; "Gao 3"), Yoshida *et al.* (*Clin. Exp.*

Immunol. 124:445-452; "Yoshida"), and Evans *et al.* (*Vaccine* 19:2080-91; "Evans"). *See*, the Office Action at pages 9 to 14. Although not acquiescing to the rejection, applicants have canceled claims 85, 88, 94, 100, 107, 115 to 117, and 119, obviating the rejection as to those claims.

As a further ground for distinguishing the pending claims over the prior art, applicants have amended claim 54 to incorporate many of the elements previously recited in claim 123, which was not included in the present obviousness rejection. The Office has not alleged, much less established, that Barnett, Nabel, Gao 1, Gao 3, Yoshida, and Evans, singly or in combination, teach or suggest every element of amended claim 54, particularly the specific nucleic acid and protein compositions to be administered in the claimed methods. Even if the general concepts of administering a polyvalent HIV vaccine were known (which applicants do not concede), there are still numerous combinations of nucleic acids and proteins of many different primary isolates, and the specific nucleic acids and proteins recited in the present claims would not have been obvious.

In addition, applicants have provided evidence of successfully inducing an immune response in the form of neutralizing antibodies against multiple HIV subtypes in both monkeys (Pal *et al.*) and humans (Wang *et al.*). Pal *et al.* describe polyvalent DNA vaccines that encode the *env* gene from four primary HIV-1 isolates: 92US715.6 (clade B), Ba-L (clade B), 96ZM651 (clade C), and 93TH976.17 (clade E) and the *gag* gene from a molecularly cloned virus NL4-3 (clade B). This composition, recited in claim 54, induced an immune response that includes neutralizing antibodies (*see*, page 344, right column). The neutralizing antibody activity is further borne out in completely protecting 4 out of 6 immunized monkeys, *i.e.*, no virus was detected after challenge, while 7 out of 7 animals in the control group had a high level viral load after challenge (*see,* Figure 6).

Applicants have also tested a DNA vaccine composition referred to as DP6-001, which is described in the present patent application and recited in claim 126, that includes six DNA plasmids that encode gp120 glycoproteins from each of the following primary isolates: subtype A, subtype B (92US715.6 and Bal), subtype C (96ZM651), and subtype E, and a sixth plasmid

encoding a gag protein, also from subtype C. This DNA vaccine composition was used to immunize healthy adult volunteers, and was followed by a protein boost composition including equal amounts of the five gp120 proteins matching those used in the DNA vaccine (*see,* Wang *et al.,* Materials and Methods, p. 3948). The results were remarkable, especially in view of the past failures of others. For example, "[P]ositive neutralizing activities against MN were seen in 100% of Groups A and B vaccines sera at the peak antibody level (after the second protein boost)" (page 3951, right column, line 4, to page 3952, left column, line 1).

Other than applicants' recent publications, applicants are aware of no other group having succeeded in generating such neutralizing antibodies in primates or humans. Although others have suggested various approaches, such as Barnett's DNA prime-protein boost approach and Nabel's multivalent modified DNA approach, and although others such as Gao 1 have described the presence of multiple different clades or subtypes of HIV, no one else has been able to achieve what applicants have claimed and then demonstrated in Phase 1 human clinical trials – the induction of an immune response from a DNA prime-protein boost HIV-1 vaccine composition. Based on these surprising results, applicants respectfully submit that claim 54 is patentable, and request that the Examiner reconsider and withdraw this rejection.

In the same way, applicants have included the main elements of claim 123 in new independent claim 126, and thus it, and its dependent claims, are also nonobvious for at least the same reasons discussed above. Applicants therefore respectfully request that this rejection be reconsidered and withdrawn and not applied to the new claims.

CONCLUSION

Applicants submit that the all of the claims are in condition for allowance and request entry of the proposed amendments and confirmation of allowance by the Examiner. It is believed that all of the pending issues have been addressed. However, the absence of a reply to a specific rejection, issue, or comment does not signify applicants' agreement. In addition, because the arguments made above may not be exhaustive, there may be additional reasons for patentability of any or all pending claims (or other claims) that have not been expressed.

Further, the amendment of any claim does not necessarily signify concession of unpatentability of the claim prior to its amendment.

The fee for the Petition for Four-Month Extension of Time for a small entity ($865) is being paid on the electronic filing system by way of deposit account authorization. Please apply any other charges or credits to Deposit Account No. 06-1050, referencing Attorney Docket No. 07917-0269001.

Respectfully submitted,

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